REMARKS

The Examiner has indicated that German Patent No. DE 39 42 728 ("the German patent") is pertinent to the claims of the present patent application because it discloses a partial amino acid sequence of pC(p22), an immunodominant outer surface protein of *Borrelia burgdorferi*. The partial sequence (p1) disclosed in the German patent is a 13 amino acid sequence which contains the amino acid sequence ATVLA, which corresponds to amino acids 91-95 of hsp65 of *M. tuberculosis*. The sequence ATVLA is a 5-mer forming part of a peptide corresponding to one species of the peptide claimed in the present application. Nevertheless, for the following reasons, the disclosure of the German patent does not teach or suggest the peptides of the present invention.

First, the pC of *Borrelia burgdorferi* is not a stress protein. Further, the p1 13-mer, or any 7-mer which can be derived therefore, is not identical to any *M. tuberculosis* 7-mer, including a peptide having the ATVLA sequence. In pertinent part, the amino acid sequences of the p1 peptide and the claimed *M. tuberculosis* hsp65 peptide are SNATVLAVK and TTATVLAQA, respectively. Under no circumstance can a 7-30-mer be derived from the p1 sequence which is identical to a peptide taken from hsp65. Thus, the claimed peptide is novel. Claim 21 is amended to clarify that the microbial protein has a mammalian stress protein homologue, unlike pC. Since the pC protein is not recognized as a stress protein and there is no indication that the p1 sequence is a T cell epitope, there is no art recognized motivation to alter the p1 sequence to yield the claimed hsp65 sequence. Therefore, the hsp65 sequence is not obvious over the p1 sequence.

Further, the partial sequence of pC listed in the German patent is incorrect. To determine the sequence of pC, pC was trypsinized and the sequence of two trypsinized peptide products, p1 and p2, was determined. The amino acid sequence of p1 is reported as KITDSNATVLAVK (emphasis added). Degenerate oligonucleotides were prepared from the identified p1 and p2 sequences and the full sequence of pC was determined. In a patent family search on INPADOC and DERWENT (copies enclosed), Applicants identified CA 2,072,008. The Canadian patent claims priority to the German patent, but provides both the sequence of p1 and the complete amino acid sequence of the pC protein. The above-mentioned protocol used to determine the pC sequence is also disclosed in this reference. The sequence of pC is listed on page 27 of the Canadian patent. Importantly, the portion of the sequence of pC corresponding to the p1 fragment here reads KITDSNAFVLAVK. For whatever reason, the German patent p1 sequence was incorrectly identified as KITDSNATVLAVK. The correctness of the Canadian patent rather than the German patent is corroborated by the three attached ENTREZ GenPept reports, listing the amino acid sequence of pC, submitted by the inventors of the German and Canadian patents, as "AFVLA" in pertinent part.

As described above, the p1 sequence does not anticipate the peptides claimed in the present application. The claimed peptides are not rendered obvious by the disclosure of the German or the Canadian patents because: 1) the p1 sequence apparently included a typographic error and therefore likely never existed; 2) even if it existed as a trypsinized fragment of pC or as published erroneous laboratory results, no skilled artisan would look to the p1 sequence to ascertain the sequence of a fragment

of pC when the later-reported sequence is available and different; 3) the disclosed p1 13-mer is a portion of a 22 kD protein and is never discussed outside of this context; 4) the pC protein is not disclosed to be a stress protein homologue; 5) no 7-30-mer corresponding to a 7-30-mer of pC is disclosed to be a T cell epitope, even if it included the ATVLA sequence of p1; and 6) there is no discussion of a use for p1 outside the context of using the sequence to prepare a degenerate oligonucleotide to deduce the sequence of pC. For these reasons, the disclosure of p1 does not anticipate or render obvious the 7-30-mer of the present application.

As a final issue, the Examiner has rejected claims 1-8, 17 and 18 for the recitation of sequence identities. Claim 1 is hereby amended to remove the actual the term "sequence identity" and the percentages of sequence identity. In view of this amendment, the Examiner's rejection for purported lack of a disclosed sequence identity algorithm is rendered moot. The term "homologue," a term suggested by the Examiner is, clearly, not indefinite because it does not require a calculation of a percentage of homology, only that the microbial and mammalian counterparts show structural and functional homology. The recitation of the term "homology" in the claims is further substantiated by the examples of the specification showing microbial proteins and their conserved mammalian stress protein homologues.

Claim 7 is redrafted as new claim 22, to remove the purported ambiguity with regard to a second microbial T cell epitope which has no corresponding mammalian counterpart.

For the reasons discussed above and in view of the Amendment submitted on March 31, 1999, Applicants believe that

claims 1, 3-6, 17, 18 , 21 and 22 define over the prior art of record and are in proper form for allowance. Applicants respectfully request allowance of claims 1, 3-6, 17, 18, 21 and 22.

Respectfully submitted,

WEBB ZIESENHEIM LOGSDON
ORKIN & HANSON, P.C.

By _____

Jesse A. Hirshman
Registration No. 40,016
Attorney for Applicants
700 Koppers Building
436 Seventh Avenue
Pittsburgh, PA 15219-1818
Telephone: 412-471-8815
Facsimile: 412-471-4094